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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/826,319	04/03/2001	Michael F. Lahn	2879-80	4155

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EXAMINER
SCHWADRON, RONALD B

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 02/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/826,319	LAHN ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-35 is/are pending in the application.

4a) Of the above claim(s) 3-8 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,2,9-35 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Claims 1,2,9-35 are under consideration.

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1,2,9-35 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Lobb et al. (US Patent 5,871,734) as evidenced by Arrhenius et al. (US Patent 5,869,448) in view of Schramm et al., Wigzell et al. (US Patent 5,958,410) and Krause et al. (US Patent Application Publication 2002/0037286) for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

Lobb et al. teach use of antibody against VLA-4 to treat asthma (see abstract). It is a property of VLA-4 that it is a receptor on T cells (see Arrhenius et al., column 63, last paragraph). AHR occurs in asthma (see column 12, Example 2). Lobb et al. teach aerosol administration of antiVLA-4 antibody (see column 12, Example 2). Lobb et al. teach use of humanized antiVLA-4 antibody (see column 5, penultimate paragraph). Said antibody does not stimulate T cell activation (said antibodies inhibit VLA-4 function, see column 7, penultimate paragraph). Lobb et al. teach use of monovalent antibody (see column 7, third paragraph). Lobb et al. teach use of antibody dosages

encompassed by those recited in claims 18 and 19 (see column 6, penultimate paragraph). Lobb et al. teach administration of said antibody in PBS via nebulized spray (see column 6, penultimate paragraph). Lobb et al. teach the method of claim 27 (see claim 17). Lobb et al. teach the method of claims 28,31,32 (see column 12, Example 2). Lobb et al. teach that the effect seen can be achieved without detectable blood levels of antibody (see column 12, last paragraph) wherein the antibody would not therefore substantially effect peripheral immune function (eg. because it was not present in the blood). Lobb et al. teach use of said method in humans (see claim 16). Lobb et al. teach that their method resulted in a 70% decrease in inhibition of late phase response which would correlate with the improved FEV1 as per claim 34. Lobb et al. do not teach use of antiTCR αβ antibodies. Schramm et al. teach use of IV antiTCR αβ antibodies to treat asthma (see abstract). Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract). Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (AKA pulmonary aerosol) administration of antiTCR antibody(see column 13, second paragraph and column 12, penultimate paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Lobb et al. teach aerosol administration of an antibody which binds T cells to treat asthma and Schramm et al. teach that a different antibody which binds T cells (antiTCR αβ) can be used to treat asthma. One of ordinary skill in the art would have been motivated to do the aforementioned because Lobb et al. teach that the anti T cell antibody can be administered in a variety of art known routes including aerosol. One of ordinary skill in the art would have also been motivated to do the aforementioned because Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (AKA pulmonary aerosol) administration of antiTCR antibody(see column 13, second paragraph and column 12, penultimate paragraph). A neutralizing antibody would have been used in the claimed method because Schramm et al. teach that asthma symptoms are reduced in the absence of TCRαβ T cells (see abstract). Regarding the particular dosages of formulation or dosage per weight, a routineer would initially test a wide variety

of different dosages in order to have determined the smallest effective dose of the antibody used. A routineer would have administered said antibody in conjunction with art known treatments for asthma such as those disclosed in column 2, first paragraph of Lobb et al. The antibody would have been administered either before or during asthma symptoms.

Regarding applicants comments, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Lobb et al. teach aerosol administration of an antibody which binds T cells to treat asthma and Schramm et al. teach that a different antibody which binds T cells (antiTCR $\alpha\beta$) can be used to treat asthma. In addition, Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (A.K.A. pulmonary aerosol) administration of antiTCR antibodies(see column 13, second paragraph and column 12, penultimate paragraph). Regarding applicants comments about motivation, Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (A.K.A. pulmonary aerosol) administration (see column 13, second paragraph and column 12, penultimate paragraph). In addition, one of ordinary skill in the art would have been motivated to do the aforementioned because Lobb et al. teach that the anti T cell antibody can be administered in a variety of art known routes including aerosol.

Regarding applicants comments about Lobb et al., Schramm et al. teach that an antibody which binds T cells (antiTCR $\alpha\beta$) can be used to treat asthma. Thus, the art recognized that an antiTCR $\alpha\beta$ could be used to treat asthma. Furthermore, Lobb et al. disclose:

"For instance, to the extent that the beneficial effects reported herein are due to the inhibition of leukocyte recruitment to VCAM-1 expressing endothelium..." (column 8, last paragraph).

Thus, Lobb et al. contemplate that their method involves inhibition of leukocytes including T cells. Lobb et al. teach use of antibody against VLA-4 to treat asthma (see abstract). VLA-4 is a receptor on T cells (see Arrhenius et al., column 63, last

paragraph). Thus, the antibody taught by Lobb et al. binds T cells. Regarding applicants comments about Schramm et al., Schramm et al. teach use of IV antiTCR αβ antibodies to treat asthma (see abstract). Schramm et al. disclose that their results indicate that acute allergic responses are dependent on intact TCRαβ T cells. The animals have asthma, receive the antiTCR antibody and the asthma related responses are resolved. Thus, the asthma is treated. Furthermore, the only actual data provided in the specification involves mouse models. Thus, it is unclear as to why the mouse data provided by Schramm et al. is any less relevant than the mouse data provided by applicant. Furthermore, there is no teaching in Schramm et al. that a complete systemic depletion of an entire T cell subset from an animal is required in the antibody treated animals. Lobb et al. teach use of antibody dosages encompassed by those recited in claims 18 and 19 (see column 6, penultimate paragraph). Regarding the particular dosages of formulation or dosage per weight, a routineer would initially test a wide variety of different dosages in order to have determined the smallest effective dose of the antibody used.

Regarding the Wigzell et al. reference, said reference discloses use of cytotoxic antiTCR antibodies which deplete T cells (see column 14, lines 4-7). Wigzell et al. teach that **pathologic T cells found in the lungs** can be treated via intrapulmonary (A.K.A. pulmonary aerosol) administration (see column 13, second paragraph and column 12, penultimate paragraph). Regarding applicants comments about evidence of the effectiveness of pulmonary administration, applicant is reminded that all art is deemed enabled in the absence of evidence to the contrary. The MPEP section 2121 discloses:

PRIOR ART IS PRESUMED TO BE OPERABLE/ ENABLING

When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. In re Sasse, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). See also MPEP § 716.07.

There is no evidence of record that the Wigzell et al. reference lacks enablement.

Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract). Krause et al. teach:

"When antibodies are used therapeutically, a preferred route of administration is by pulmonary aerosol.".

This statement is not limited to a particular antibody taught by Krause et al. In addition, as per above, there is no evidence of record that the Krause et al. reference is not enabled.

AHR occurs in asthma (see column 12, Example 2). Lobb et al. teach aerosol administration of antiVLA-4 antibody (see column 12, Example 2). Lobb et al. teach use of humanized antiVLA-4 antibody (see column 5, penultimate paragraph). One of ordinary skill in the art would have been motivated to do the aforementioned because Lobb et al. teach that the anti T cell antibody can be administered in a variety of art known routes including aerosol. One of ordinary skill in the art would have also been motivated to do the aforementioned because Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (A.K.A. pulmonary aerosol) administration of antiTCR antibody(see column 13, second paragraph and column 12, penultimate paragraph).

Regarding applicants comments about Fahy et al., the comments in page 9 of said reference indicate that the reason that their antibody was not effective was because it was an antibody that bound a soluble antigen (IgE) present in large quantities in the vascular space wherein said IgE acted as a "sink of IgE". Fahy et al. hypothesize that the antibody might have been more immunogenic via the aerosol route, but the successful results of Lobb et al. would tend to disagree with this hypothesis. The issue of noncompliant patients is not germane to the instant discussion. The hypothesis that aerosolized antibody was not delivered in sufficient quantity to the lower airways seems unlikely as a potential problem for the claimed invention because the successful results of Lobb et al. would tend to disagree with this hypothesis. Therefore, the most likely explanation for the results found by Fahy et al. is that their antibody was not effective was because it was antibody that bound a soluble antigen (IgE) present in large quantities in the vascular space wherein said IgE acted as a "sink of IgE". The antibody

used in the claimed invention does not bind a soluble antigen. The antibody used in the claimed invention binds alphabeta TCR found on the surface of T cells. There is no evidence of record that soluble TCR is found in large quantities in the vascular space wherein said TCR acted as a "sink". Therefore, the results of Fahy et al. are not germane to the claimed invention. Furthermore, Lobb et al. teach aerosol administration of an antibody which binds T cells to treat asthma. In addition, Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (AKA pulmonary aerosol) administration of antiTCR antibody. (see column 13, second paragraph and column 12, penultimate paragraph). Regarding reasonable expectation of success, Lobb et al. teach aerosol administration of an antibody which binds T cells to treat asthma and Schramm et al. teach that a different antibody which binds T cells (antiTCR $\alpha\beta$) can be used to treat asthma. Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (A.K.A. pulmonary aerosol) administration of antiTCR antibody(see column 13, second paragraph and column 12, penultimate paragraph). Schramm et al. has already demonstrated that antiTCR$\alpha\beta$ antibody can be used to treat asthma. Lobb et al. have already used pulmonary administration of antibodies which bind T cells to treat asthma. Regarding applicants comments about low dosage, the only claims that recited a dosage are claims 18-23. The dosages of claims 18 and 19 are taught by Lobb et al. Thus, applicants comments regarding dosage are irrelevant to claims other than 20-23.

The claimed invention encompasses a method of treating humans, but there is no disclosure in the specification of evidence that the dosages used in claims 20-23 would have any effect in humans. Thus, to the extent that applicant is arguing unexpected results, the results disclosed in the specification are not commensurate with the scope of the claimed invention.

Regarding applicants comments about the cellular specificity of the antigen bound by the antiVLA-4 antibody, given that said antibody binds T cells and that the antibody used by Schramm et al. binds T cells (antiTCR ab) and can be used to treat asthma, it is reasonable to conclude that the method of Lobb et al. using aerosol administration

could be practiced using the antibody used by Schramm et al. that binds T cells (antiTCR αβ). Regarding applicants comments about advantages of the claimed invention, Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (AKA pulmonary aerosol) administration of antiTCR antibodies(see column 13, second paragraph and column 12, penultimate paragraph). Regarding applicants comments about gamma/delta T cells, said species is not the elected species and is not currently under examination.

5. No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday to Thursday from 7:30am to 6:00pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at 571 272 0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For

more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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